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CLAIMS

What is claimed is:

- 5 1. An isolated and purified protein product comprising an amino acid sequence selected from the group consisting of:
 - a) Figure 3 (SEQ ID NO:___),
 - b) amino acid residues 81 through 224 of Figure 3 (SEQ ID NO:___),
 - c) amino acid residues 109 through 224 of Figure 3 (SEQ ID NO:___),
 - 10 d) amino acid residues 112 through 224 of Figure 3 (SEQ ID NO:___),
 - e) amino acid residues 119 through 224 of Figure 3 (SEQ ID NO:___),
 - f) amino acid residues 129 through 224 of Figure 3 (SEQ ID NO:___),
 - g) Figure 7 (SEQ ID NO:___),
 - h) amino acid residues 81 through 228 of Figure 7 (SEQ ID NO:___),
 - 15 i) amino acid residues 89 through 228 of Figure 7 (SEQ ID NO:___),
 - j) amino acid residues 113 through 228 of Figure 7 (SEQ ID NO:___),
 - k) amino acid residues 116 through 228 of Figure 7 (SEQ ID NO:___),
 - l) amino acid residues 133 through 228 of Figure 7 (SEQ ID NO:___),
 - m) Figure 18 (SEQ ID NO:___),
 - 20 n) amino acid residues PPP through CLG of Figure 18 (SEQ ID NO:___),
 - o) amino acid residues AAR through CLG of Figure 18 (SEQ ID NO:___),
 - p) amino acid residues AGXaa through CLG of Figure 18 (SEQ ID NO:___), and
 - q) amino acid residues LRS through CLG of Figure 18 (SEQ ID NO:___).
- 25 2. A protein product of Claim 1 which is glycosylated.
3. A protein product of Claim 1 which is non-glycosylated.
4. A pharmaceutical composition comprising a mixture of a protein product of claim
- 30 1, 2 or 3 and a pharmaceutically acceptable carrier.
5. An isolated polynucleotide molecule which encodes a protein product that is at

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least 82% identical in amino acid sequence to a protein product of claim 1, wherein said protein product binds GDNF family receptor-alpha-3 (GFR α -3), and wherein said percent identity is determined by GAP, BLAST or FASTA using standard default parameters.

- 5 6. An isolated polynucleotide molecule which encodes a protein product that is at least 90% identical in amino acid sequence to a protein product of claim 1, wherein said protein product binds GDNF family receptor-alpha-3 (GFR α -3), and wherein said percent identity is determined by BLASTP using standard default parameters.
- 10 7. An isolated polynucleotide molecule selected from the group consisting of:
- a) a molecule comprising the nucleotides of Figure 2 (SEQ ID NO:__) or its complement,
 - b) a molecule encoding a polypeptide comprising amino acid residues 81 through 224 of Figure 3 (SEQ ID NO:__),
 - 15 c) a molecule encoding a polypeptide comprising amino acid residues 109 through 224 of Figure 3 (SEQ ID NO:__),
 - d) a molecule encoding a polypeptide comprising amino acid residues 112 through 224 of Figure 3 (SEQ ID NO:__),
 - e) a molecule encoding a polypeptide comprising amino acid residues 119 through 20 224 of Figure 3 (SEQ ID NO:__),
 - f) a molecule encoding a polypeptide comprising amino acid residues 129 through 224 of Figure 3 (SEQ ID NO:__),
 - g) a molecule comprising the nucleotides of Figure 6 (SEQ ID NO:__) or its complement,
 - 25 h) a molecule encoding a polypeptide comprising amino acid residues 81 through 228 of Figure 7 (SEQ ID NO:__),
 - i) a molecule encoding a polypeptide comprising amino acid residues 89 through 228 of Figure 7 (SEQ ID NO:__),
 - j) a molecule encoding a polypeptide comprising amino acid residues 113 through 30 228 of Figure 7 (SEQ ID NO:__),
 - k) a molecule encoding a polypeptide comprising amino acid residues 116 through

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- 228 of Figure 7 (SEQ ID NO:___),
- l) a molecule encoding a polypeptide comprising amino acid residues 133 through 228 of Figure 7 (SEQ ID NO:___),
 - m) a molecule encoding a protein product comprising an amino acid sequence of Figure 3 (SEQ ID NO:___),
 - n) a molecule encoding a protein product comprising an amino acid sequence of Figure 7 (SEQ ID NO:___), and
 - o) a molecule encoding a protein product comprising an amino acid sequence of Figure 18 (SEQ ID NO:___)
 - p) a molecule encoding a protein product comprising amino acid residues PPP through CLG of Figure 18 (SEQ ID NO:___),
 - q) a molecule encoding a protein product comprising amino acid residues AAR through CLG of Figure 18 (SEQ ID NO:___),
 - r) a molecule encoding a protein product comprising amino acid residues AGXaa through CLG of Figure 18 (SEQ ID NO:___), and
 - s) a molecule encoding a protein product comprising amino acid residues LRS through CLG of Figure 18 (SEQ ID NO:___).
8. An isolated polynucleotide molecule selected from the group consisting of:
- a) a molecule which hybridizes under stringent conditions to a complementary sequence of a polynucleotide molecule of Claim 5; and
 - b) a molecule which but for the degeneracy of the genetic code would hybridize under stringent conditions to a complementary sequence of a polynucleotide molecule of Claim 5,
- and wherein said isolated polynucleotide molecule encodes a protein product that binds GDNF family receptor-alpha-3 (GFR α -3).
9. A vector comprising a polynucleotide molecule according to claim 5, 6, 7 or 8.
10. A vector according to claim 9, further comprising one or more operational elements capable of effecting the amplification or expression of said polynucleotide molecule.

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11. A vector comprising polynucleotide molecule selected from the group consisting of:
- a) a molecule encoding a polypeptide comprising amino acid residues 81 through 224 of Figure 3 (SEQ ID NO:___),
 - 5 b) a molecule encoding a polypeptide comprising amino acid residues 109 through 224 of Figure 3 (SEQ ID NO:___),
 - c) a molecule encoding a polypeptide comprising amino acid residues 112 through 224 of Figure 3 (SEQ ID NO:___),
 - d) a molecule encoding a polypeptide comprising amino acid residues 119 through 10 224 of Figure 3 (SEQ ID NO:___),
 - e) a molecule encoding a polypeptide comprising amino acid residues 129 through 224 of Figure 3 (SEQ ID NO:___),
 - f) a molecule encoding a polypeptide comprising amino acid residues 81 through 228 of Figure 7 (SEQ ID NO:___),
 - 15 g) a molecule encoding a polypeptide comprising amino acid residues 89 through 228 of Figure 7 (SEQ ID NO:___),
 - h) a molecule encoding a polypeptide comprising amino acid residues 113 through 228 of Figure 7 (SEQ ID NO:___),
 - i) a molecule encoding a polypeptide comprising amino acid residues 116 through 20 228 of Figure 7 (SEQ ID NO:___),
 - j) a molecule encoding a polypeptide comprising amino acid residues 133 through 228 of Figure 7 (SEQ ID NO:___),
 - k) a molecule encoding a protein product comprising amino acid residues PPP through CLG of Figure 18 (SEQ ID NO:___),
 - 25 l) a molecule encoding a protein product comprising amino acid residues AAR through CLG of Figure 18 (SEQ ID NO:___),
 - m) a molecule encoding a protein product comprising amino acid residues AGXaa through CLG of Figure 18 (SEQ ID NO:___), and
 - n) a molecule encoding a protein product comprising amino acid residues LRS 30 through CLG of Figure 18 (SEQ ID NO:___).
12. A genetically engineered host cell comprising a polynucleotide molecule according

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to claim 5, 6, 7 or 8.

13. An isolated host cell comprising a polynucleotide molecule according to claim 5, 6, 7 or 8.

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14. A genetically engineered host cell which expresses a protein product comprising an amino acid sequence selected from the group consisting of:

- a) an amino acid sequence of Figure 3 (SEQ ID NO:__),
- b) amino acid residues 81 through 224 of Figure 3 (SEQ ID NO:__),
- 10 c) amino acid residues 109 through 224 of Figure 3 (SEQ ID NO:__),
- d) amino acid residues 112 through 224 of Figure 3 (SEQ ID NO:__),
- e) amino acid residues 119 through 224 of Figure 3 (SEQ ID NO:__),
- f) amino acid residues 129 through 224 of Figure 3 (SEQ ID NO:__),
- g) an amino acid sequence of Figure 7 (SEQ ID NO:__),
- 15 h) amino acid residues 81 through 228 of Figure 7 (SEQ ID NO:__),
- i) amino acid residues 89 through 228 of Figure 7 (SEQ ID NO:__),
- j) amino acid residues 113 through 228 of Figure 7 (SEQ ID NO:__),
- k) amino acid residues 116 through 228 of Figure 7 (SEQ ID NO:__),
- l) amino acid residues 133 through 228 of Figure 7 (SEQ ID NO:__),
- 20 m) an amino acid sequence of Figure 18 (SEQ ID NO:__),
- n) amino acid residues PPP through CLG of Figure 18 (SEQ ID NO:__),
- o) amino acid residues AAR through CLG of Figure 18 (SEQ ID NO:__),
- p) amino acid residues AGXaa through CLG of Figure 18 (SEQ ID NO:__), and
- q) amino acid residues LRS through CLG of Figure 18 (SEQ ID NO:__),
- 25 and wherein said protein product is capable of binding GDNF family receptor-alpha-3 (GFR α -3).

15. A genetically engineered host cell comprising a vector of claim 10.

30 16. A genetically engineered host cell of Claim 12 wherein said cell is suitable for human implantation and wherein said cell expresses and secretes said polynucleotide molecule.

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17. An isolated host cell of Claim 13 wherein said cell is suitable for human implantation.
- 5 18. An isolated host cell of Claim 16 or 17 wherein said cell is enclosed in a semipermeable membrane suitable for human implantation.
19. A method for the production of a protein product which is capable of binding to GDNF family receptor-alpha-3 ($\text{GFR}\alpha\text{-3}$), said method comprising the steps of:
- 10 (a) culturing a host cell comprising an isolated polynucleotide molecule according to claim 5, 6, 7 or 8, under conditions suitable for the expression of said protein product by said host cell; and
- (b) optionally, isolating said protein product expressed by said host cell.
- 15 20. A method for the production of a protein product which is capable of binding to GDNF family receptor-alpha-3 ($\text{GFR}\alpha\text{-3}$), said method comprising the steps of:
- (a) culturing an isolated host cell comprising a polynucleotide molecule encoding a protein product according to claim 1, under conditions suitable for the expression of said protein product by said host cell; and
- 20 (b) optionally, isolating said protein product expressed by said host cell.
21. A method of claim 19, wherein said polynucleotide molecule encodes a protein product comprising:
- a) amino acid residues 81 through 224 of Figure 3 (SEQ ID NO:___),
- 25 b) amino acid residues 109 through 224 of Figure 3 (SEQ ID NO:___),
- c) amino acid residues 112 through 224 of Figure 3 (SEQ ID NO:___),
- d) amino acid residues 119 through 224 of Figure 3 (SEQ ID NO:___), or
- e) amino acid residues 129 through 224 of Figure 3 (SEQ ID NO:___).
- 30 22. A method of claim 19, wherein said polynucleotide molecule encodes a protein product comprising:

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- a) amino acid residues 81 through 228 of Figure 7 (SEQ ID NO:___),
 - b) amino acid residues 89 through 228 of Figure 7 (SEQ ID NO:___),
 - c) amino acid residues 113 through 228 of Figure 7 (SEQ ID NO:___),
 - d) amino acid residues 116 through 228 of Figure 7 (SEQ ID NO:___),
 - 5 e) amino acid residues 133 through 228 of Figure 7 (SEQ ID NO:___),
 - f) amino acid residues PPP through CLG of Figure 18 (SEQ ID NO:___),
 - g) amino acid residues AAR through CLG of Figure 18 (SEQ ID NO:___),
 - h) amino acid residues AGXaa through CLG of Figure 18 (SEQ ID NO:___), or
 - i) amino acid residues LRS through CLG of Figure 18 (SEQ ID NO:___).
- 10 23. An isolated and purified protein product prepared according to the method of claim 19.
24. An isolated and purified protein product prepared according to the method of
- 15 claim 20.
25. A protein product which is capable of binding to GDNF family receptor-alpha-3 (GFR α -3), prepared by a method comprising the steps of:
- (a) culturing a host cell containing a polynucleotide molecule selected from the group
- 20 consisting of:
- i) a molecule comprising the nucleotides of Figure 2 (SEQ ID NO:___) or its complement,
 - ii) a molecule encoding a polypeptide comprising amino acid residues 81 through 224 of Figure 3 (SEQ ID NO:___),
 - 25 iii) a molecule encoding a polypeptide comprising amino acid residues 109 through 224 of Figure 3 (SEQ ID NO:___),
 - iv) a molecule encoding a polypeptide comprising amino acid residues 112 through 224 of Figure 3 (SEQ ID NO:___),
 - v) a molecule encoding a polypeptide comprising amino acid residues 119 through
 - 30 224 of Figure 3 (SEQ ID NO:___),
 - vi) a molecule encoding a polypeptide comprising amino acid residues 129 through 224 of Figure 3 (SEQ ID NO:___),

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- vii) a molecule comprising the nucleotides of Figure 6 (SEQ ID NO:__) or its complement,
- viii) a molecule encoding a polypeptide comprising amino acid residues 81 through 228 of Figure 7 (SEQ ID NO:__),
- 5 ix) a molecule encoding a polypeptide comprising amino acid residues 89 through 228 of Figure 7 (SEQ ID NO:__),
- x) a molecule encoding a polypeptide comprising amino acid residues 113 through 228 of Figure 7 (SEQ ID NO:__),
- 10 xi) a molecule encoding a polypeptide comprising amino acid residues 116 through 228 of Figure 7 (SEQ ID NO:__),
- xii) a molecule encoding a polypeptide comprising amino acid residues 133 through 228 of Figure 7 (SEQ ID NO:__),
- xiii) a molecule encoding a protein product comprising an amino acid sequence of Figure 3 (SEQ ID NO:__),
- 15 xiv) a molecule encoding a protein product comprising an amino acid sequence of Figure 7 (SEQ ID NO:__), and
- xv) a molecule encoding a protein product comprising an amino acid sequence of Figure 18 (SEQ ID NO:__),
- xvi) a molecule encoding a protein product comprising an amino acid residues PPP through CLG of Figure 18 (SEQ ID NO:__),
- 20 xvii) a molecule encoding a protein product comprising an amino acid residues AAR through CLG of Figure 18 (SEQ ID NO:__),
- xviii) a molecule encoding a protein product comprising an amino acid residues AGXaa through CLG of Figure 18 (SEQ ID NO:__), and
- 25 xix) a molecule encoding a protein product comprising an amino acid residues LRS through CLG of Figure 18 (SEQ ID NO:__)
- under conditions suitable for the expression of said protein product by said host cell; and
- (b) optionally, isolating said protein product expressed by said host cell.
- 30 26. An antibody that binds to a peptide comprising an amino acid sequence of Figure 3 (SEQ ID NO:__), Figure 7 (SEQ ID NO:__) or Figure 18 (SEQ ID NO:__).

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27. The antibody of claim 26 wherein said antibody is a monoclonal antibody.
28. The antibody of claim 26 wherein said antibody is a polyclonal antibody.
- 5 29. An antibody produced by immunizing an animal with a peptide comprising an amino acid sequence of Figure 3 (SEQ ID NO:___), Figure 7 (SEQ ID NO:___) or Figure 18 (SEQ ID NO:___).
30. A hybridoma that produces a monoclonal antibody that binds to a peptide
10 comprising an amino acid sequence of Figure 3 (SEQ ID NO:___), Figure 7 (SEQ ID NO:___) or Figure 18 (SEQ ID NO:___).
31. A device, comprising:
- (a) a membrane suitable for implantation; and
- 15 (b) cells encapsulated within said membrane, wherein said cells secrete a protein product of claim 1;
said membrane being permeable to said protein product and impermeable to materials detrimental to said cells.
- 20 321. A device, comprising:
- (a) a membrane suitable for implantation; and
- (b) cells encapsulated within said membrane, wherein said cells contain a polynucleotide molecule selected from the group consisting of:
- i) a molecule comprising the nucleotides of Figure 2 (SEQ ID NO:___),
- 25 ii) a molecule comprising the nucleotides of Figure 6 (SEQ ID NO:___),
- iii) a molecule encoding a protein product comprising amino acid residues 81 through 228 of Figure 7 (SEQ ID NO:___),
- iv) a molecule encoding a protein product comprising amino acid residues 89 through 228 of Figure 7 (SEQ ID NO:___),
- 30 v) a molecule encoding a protein product comprising amino acid residues 113 through 228 of Figure 7 (SEQ ID NO:___),
- vi) a molecule encoding a protein product comprising amino acid residues 116

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- through 228 of Figure 7 (SEQ ID NO:__),
- vii) a molecule encoding a protein product comprising amino acid residues 133 through 228 of Figure 7 (SEQ ID NO:__),
- viii) a molecule encoding a protein product comprising amino acid residues PPP through CLG of Figure 18 (SEQ ID NO:__),
- 5 ix) a molecule encoding a protein product comprising amino acid residues AAR through CLG of Figure 18 (SEQ ID NO:__),
- x) a molecule encoding a protein product comprising amino acid residues AGXaa through CLG of Figure 18 (SEQ ID NO:__), and
- 10 xi) a molecule encoding a protein product comprising amino acid residues LRS through CLG of Figure 18 (SEQ ID NO:__),
- wherein said cells express and secrete said protein product,
- and wherein said membrane is permeable to said protein product and impermeable to materials detrimental to said cells.

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33. The use of the isolated and purified protein product of claim 1 for the manufacture of a pharmaceutical composition.
34. A pharmaceutical composition comprising a protein product of claim 1 in
- 20 combination with a pharmaceutically acceptable carrier.